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The Nature of the Micellar Stern Region As Studied by Reaction Kinetics. 2[†,1]

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The nature of rate-retarding effects of cationic micelles on the water-catalyzed hydrolyses of a series of para-substituted 1-benzoyl-1,2,4-triazoles (**1a**−**f**) and 1-benzoyl-3-phenyl-1,2,4-triazole (**2**) has been studied using kinetic methods. A comparison is drawn between medium effects in the micellar Stern region and in model solutions for the micellar Stern region. Simple model solutions involving concentrated aqueous solutions of a small ionic molecule resembling the surfactant headgroup, as reported before,[1] were improved. New model solutions for alkyltrimethylammonium bromide micelles contain both tetramethylammonium bromide (TMAB), mimicking micellar headgroups, and 1-propanol, mimicking hydrophobic tails. The rate-retarding effect of micelles on the hydrolysis of **1a**−**f** and **2** is caused by the high concentration of headgroups as well as by hydrophobic tails in the Stern region where **1a**−**f** and **2** bind to the micelle. Individual contributions of these interactions are quantified. Rate-retarding effects found for different probes, with different sensitivities for interactions as they occur when the probe binds to the micellar Stern region, as well as the micellar Stern region's micropolarity as reported by the $E_T(30)$ probe, are satisfactorily reproduced by new model solutions containing both TMAB and 1-propanol.

Introduction

Micelle-forming surfactants self-aggregate in a cooperative manner, forming stable but highly dynamic clusters above the critical micelle concentration (cmc). Gruen described a realistic model for a micelle[2] which involves a rather sharp interface between two distinctly different "zones" making up a micelle: (i) a dry[2,3] hydrophobic hydrocarbon core surrounded by (ii) a region filled with surfactant headgroups, part of the counterions (in case of ionic surfactants) and water, viz. the Stern region. The Stern region is an interfacial region between the hydrocarbon core and bulk water (the third "zone" in micellar solutions). This model has been validated for both ionic and nonionic micelles using molecular dynamics simulations.[4,5]

In micellar solutions, reactions can be either accelerated or inhibited compared to the reaction in aqueous solutions without added cosolutes.[6−8] Remarkable success in enhancing reaction rates[9] introducing catalytic moieties in surfactants has been achieved.[10] However, we limit discussion solely to "medium effects" as they occur in solutions of unfunctionalized micelle-forming amphiphiles.

The exact mechanism of micellar acceleration and deceleration has remained obscure because a good description of the local reaction environment offered by micellar binding sites, often referred to as the "micellar pseudophase", is lacking. The present (and our previous[1]) study investigated mechanistic aspects of micellar effects on water-catalyzed hydrolysis reactions to develop a satisfactory description of the micellar pseudophase as a reaction medium. Nevertheless, the distinct differences between micellar core and Stern region make it impossible to describe the complete micelle as a homogeneous "entity" or "(pseudo)phase". Descriptions of medium effects exerted by micelles describe either the Stern region or the hydrocarbon core, depending on the binding location of the (reactive) probes that are used.

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(1) Part 1: Buurma, N. J.; Herranz, A. M.; Engberts, J. B. F. N. *J. Chem. Soc., Perkin Trans. 2* **1999**, 113−119.

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(8) Engberts, J. B. F. N. *Pure Appl. Chem.* **1992**, *64*, 1653−1660.

(9) The difference between reaction rates and reaction rate constants should be noted. Due to compartmentalization, concentrations of reactants inside micelles can be higher so that, notwithstanding lower reaction rate constants, reaction rates can still be higher than observed in bulk water.

(10) Examples of surfactants equipped with catalytically active headgroups can be found among others in the following: (a) Otto, S.; Engberts, J. B. F. N.; Kwak, J. C. T. *J. Am. Chem. Soc.* **1998**, *120*, 9517−9525. (b) Sirieix, J.; de Viguerie, N.; Riviere, M.; Lattes, A. *New J. Chem.* **1999**, *23*, 103−109. (c) Ghosh, K. K.; Pandey, A.; Roy, S. *J. Phys. Org. Chem.* **1999**, *12*, 493−498. (d) Tagaki, W.; Chigira, M.; Amada, T.; Yano, Y. *J. Chem. Soc., Chem. Commun.* **1972**, 219−220.

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A prerequisite for understanding the reaction medium offered by micelles is to know where reaction occurs. A micelle offers several binding sites for relatively apolar molecules. These include the hydrophobic core and hydrophobic binding sites located in the Stern region. The latter region is particularly flexible in binding molecules as it contains, apart from water molecules, highly hydrophilic surfactant headgroups and hydrophobic domains due in part to backfolding of surfactant tails.[2−4] In our previous study,[1] we showed that the water-catalyzed hydrolysis reactions of activated amides take place in the micellar Stern region. This conclusion agrees with the binding locations found using a variety of techniques for many other, especially aromatic, molecules.[11]

In view of the literature evidence mentioned above, the kinetic probes used in the study reported here almost certainly bind in the micellar Stern region. Hence, the experiments effectively provide information about the reaction medium properties of the Stern region. The aim of this study was to model the medium properties of the micellar Stern region in terms of aqueous solutions comprising compounds mimicking molecules and parts of molecules present in the Stern region.

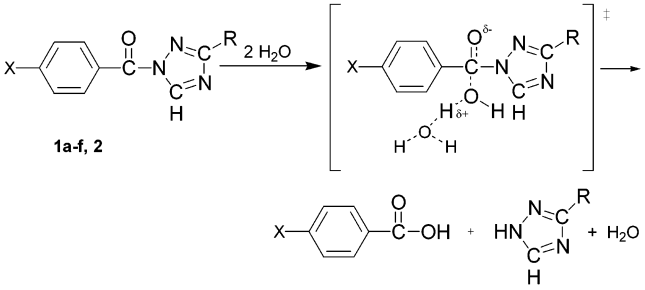
A key feature of the micellar Stern region is the concentration of headgroups and counterions. The concentration of headgroups in the Stern region[12−14] lies in the range of 3−5 mol dm^{-3}, though recent work suggested lower values.[15] In our previous work, we determined upper limits for the concentration of headgroups in the Stern regions of *n*-dodecyltrimethylammonium bromide (DTAB), *n*-hexadecyltrimethylammonium bromide (CTAB), and sodium *n*-dodecyl sulfate (SDS) of approximately 4 M.[1] The concentration of counterions is slightly less due to incomplete counterion binding, locally creating an electrically nonneutral environment.

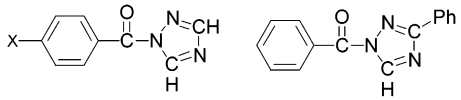
In our preceding study,[1] we showed that rate-retarding effects exerted by micelles on certain hydrolysis reactions can be largely explained in terms of salt effects. However, the success of modeling the micellar Stern region using a concentrated salt solution depends on the reaction chosen to probe the Stern region's properties as a reaction medium.[1,16] In this study we incorporate in the mimic both polar and apolar components with the aim of inducing medium effects still more representative of the Stern region.

A Kinetic Model for Reactions in Micellar Solutions

The hydrolytic reactions described here are the water-catalyzed, pH-independent hydrolysis reactions of substituted 1-benzoyl-1,2,4-triazoles (**1a**−**f**) and 1-benzoyl-3-phenyl-1,2,4-triazole (**2**).

SCHEME 1





1a X=MeO, **b** X=Me, **c** X=H, **d** X=Cl, **e** X=CF_3O, **f** X=NO_2 **2**

The reactions proceed via a dipolar activated complex in which two water molecules, one acting as a nucleophile and the other as a general base, are involved *with three protons in flight* (Scheme 1).[17−19]

Kinetic data for reactions in micellar solutions are analyzed using eq 1 in a nonlinear least-squares fitting procedure. Equation 1 represents the nonlinear form of the Menger−Portnoy equation:[20]

$$k_{obsd} = \frac{k(m_c = 0) + k_{mic}K_m([surf] - cmc)/N}{1 + K_m([surf] - cmc)/N} \quad (1)$$

Here k_{obsd} is the observed rate constant at a surfactant concentration [surf], $k(m_c = 0)$ is the rate constant in water without added cosolute (pH = 4.0),[21] and k_{mic} is the rate constant under conditions of complete binding of the substrate to the micelles. For the present system, the micellar rate constant k_{mic} is the rate constant for reaction in the micellar Stern region. N is the aggregation number of the micelle, K_m is the binding constant of the kinetic probe to the micelle (the kinetic probe residing in the Stern region), and cmc is the critical micelle concentration of the surfactant.

In addition to micellar rate constants k_{mic} and micellar binding constants K_m, transition-state pseudoequilibrium constants K^{AC} can be determined.[22,23] Transition-state pseudoequilibrium constants K^{AC} are hypothetical bind-

(11) See, for example: (a) Menger, F. M. *Acc. Chem. Res.* **1979**, *12*, 111−117. (b) Vitha, M. F.; Dallas, A. J.; Carr, P. W. *J. Phys. Chem.* **1996**, *100*, 5050−5062 and references therein.
(12) Bunton, C. A.; Nome, F.; Quina, F. H.; Romsted, L. S. *Acc. Chem. Res.* **1991**, *24*, 357−364.
(13) Mukerjee, P. *J. Phys. Chem.* **1962**, *66*, 943−945.
(14) Menger, F. M.; Yoshinaga, H.; Venkatasubban, K. S.; Das, A. R. *J. Org. Chem.* **1981**, *46*, 415−419.
(15) (a) Chaudhuri, A.; Loughlin, J. A.; Romsted, L. S.; Yao, J. H. *J. Am. Chem. Soc.* **1993**, *115*, 8351−8361. (b) Soldi, V.; Keiper, J.; Romsted, L. S.; Cuccovia, I. M.; Chaimovich, H. *Langmuir* **2000**, *16*, 59−71.
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(17) Fife, T. H.; McMahon, D. M. *J. Am. Chem. Soc.* **1969**, *91*, 7481−7485.
(18) Karzijn, W.; Engberts, J. B. F. N. *Tetrahedron Lett.* **1978**, 1787−1790.
(19) Engbersen, J. F. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1975**, *97*, 1563−1568.
(20) Menger, F. M.; Portnoy, C. E. *J. Am. Chem. Soc.* **1967**, *89*, 4698−4703.
(21) For the present reactions, the minor decrease in rate constant before the cmc indicates that rate-retarding effects below the cmc are small, justifying our choice of $k(m_c = 0)$. It should also be noted that micellar rate constants for substrates bound to spherical micelles can only be determined as long as the surfactant concentration is below the concentration at which wormlike micelles start to form. This poses an upper limit on the concentration range in which relevant results can be obtained.
(22) Kurz, J. L. *J. Am. Chem. Soc.* **1963**, *85*, 987−991.
(23) Kraut, J. *Science* **1988**, *242*, 533−540.

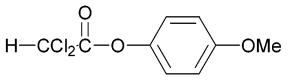
ing constants of the activated complex to the micelle. For the system under study, K^{AC} is given by eq 2.

$$K^{AC} = \frac{k_{mic}K_m}{k(m_c = 0)} = \frac{k_{mic}'[H_2O]_{mic}^{\ 2}K_m}{k_w'[H_2O]_w^{\ 2}} \qquad (2)$$

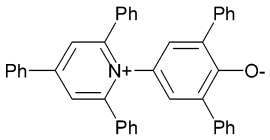
In eq 2, k_w' and k_{mic}' are the third-order rate constants (rate of reaction of probe P: $d[P]/dt = k_z'[P][H_2O]_z^2$, where z represents subscripts mic and w in eq 2) in bulk water and in the micellar Stern region, respectively. $[H_2O]_w$ is the water concentration in water, and $[H_2O]_m$ is the water concentration in the micelle, i.e. in the Stern region.

An Extended Model of the Micellar Stern Region

Concentrated salt solutions may effectively reproduce the medium effects exerted by the micellar Stern region on one (series of) probe(s) but not on another series. For example, medium effects on the solvatochromic $E_T(30)$ probe[24] in the Stern region cannot be accounted for solely on the basis of the polarity of a concentrated salt solution.[1]



3



$E_T(30)$

Similarly, the hydrolysis of phenyl chloromethanoate is not nearly as much retarded in salt solutions as in micellar solutions.[16] Another indication is the failure of **3**, a hydrolytic probe that is particularly sensitive to hydrophobic interactions, to show a relation between the charge of the Stern region and the rate-retarding effect,[1] as was also observed by others for the hydrolysis of 4-nitrophenyl 2,2-dichloropropanoate.[25,26]

If the $E_T(30)$ probe is a good micropolarity reporter, the micropolarity of the micellar Stern region is considerably lower than expected on the basis of the concentrated salt solutions used as mimics of the Stern region. This lower polarity is envisaged to be primarily caused by interactions of the probes with the hydrophobic tails of the surfactants in the Stern region.

In this context, we chose the hydrolysis of a series of substituted 1-benzoyl-1,2,4-triazoles **1a**−**f**[27] in the presence of micelles of DTAB and CTAB for detailed analysis. The Stern region of micelles of ionic surfactants is modeled by including both hydrophobic and ionic interactions. Our new model solutions contain both salt, mimicking ionic interactions, and 1-propanol, mimicking hydrophobic interactions.[28] We separate the effect of the ionic headgroups and of the hydrophobic tails leading to a satisfactory reproduction of the behavior of all tested probes. It should be noted that ionic interactions do not only include the effect of the charges of the surfactant headgroups[29] but instead are defined to include all rate-influencing effects of the surfactant headgroups, i.e. charge, effect on local water activity, and direct 1:1 interactions with the hydrolytic probe.

TABLE 1. Overview of the Hydrolysis Rate Constants of 1-Benzoyl-1,2,4-triazoles 1a−f at 298.15 K

probe	σ_p^{30}	$k_x(m_c = 0)/10^{-4}$ s^{-1}
1a	−0.28	4.1
1b	−0.14	9.4
1c	+0.00	21.2
1d	+0.24	36.0
1e	+0.32	43.1
1f	+0.81	278

Results and Discussion

Rate constants for hydrolysis of **1a**−**f** in water without added cosolutes, $k_x(m_c = 0)$, together with the Hammett substituent constants σ_p^{30} are summarized in Table 1 (subscript x indicates the probe molecule).

It is shown that the rate of hydrolysis increases with increasing electron-withdrawing ability of the para-substituent, as expected for a reaction in which a (partial) negative charge develops on the carbonyl group going toward the activated complex (Scheme 1). The hydrolysis of all of these probes is retarded in solutions containing micelles of CTAB and DTAB (examples given in Figure 1).

From a nonlinear least-squares fit to eq 1, micellar rate constants for hydrolysis and micellar binding constants were determined (Table 2).

There is no appreciable trend in the micellar binding constants of **1a**−**f** (Table 2) with substituent constant (Table 1). However, micellar binding constants for CTAB on average are about three times larger than those for DTAB. For comparison of the rate-retarding effects on the hydrolysis of the individual hydrolytic probes, the relative rate constants of hydrolysis in aqueous solutions of DTAB and CTAB and the logarithms of these relative rate constants are given in Table 3.

For **1d**−**f**, micelles of CTAB retard hydrolysis more than micelles of DTAB. However, micelles of DTAB retard the hydrolysis of **1a**,**b** more compared with micelles of CTAB (Table 3). Apart from these rather unusual rate effects, $\ln(k_{x,mic}/k_x(m_c = 0))$ tends to increase (decrease in absolute value) with increasing σ_p.

We improved our previous model for the micellar Stern region[1] by adding a compound mimicking the interactions with the alkyl tails of the surfactants. 1-Propanol was used as added cosolute being the highest linear[32] alcohol

(24) Reichardt, C. *Chem. Rev.* **1994**, *94*, 2319−2358.
(25) El Seoud, O. A.; Ruasse, M. F.; Possidonio, S. *J. Phys. Org. Chem.* **2001**, *14*, 526−532.
(26) In our opinion, the conclusion in ref 25 that the rate-retarding effect brought about by the micelles is not a salt effect is unwarranted. The conclusion has been based on activation parameters of the reaction occurring in the micelle. However, these activation parameters will include effects of the thermodynamics of micellization changing with temperature.
(27) A series of probes with different substituents was used before in a study of micellar medium effects in terms of Hammett ρ-values. See: Brinchi, L.; Di Profio, P.; Germani, R.; Savelli, G.; Spreti, N.; Bunton, C. A. *Eur. J. Org. Chem.* **2000**, 3849−3854.
(28) Recently, similar attempts at including both "headgroup mimics" and "tail mimics" in model solutions for the micellar Stern region have been made. However, these tertiary solutions either (i) do not distinguish between the rate effects of headgroup mimic and tail mimic (refs 25 and 40) or (ii) seem to reproduce the rate of a single reaction only (Tada, E. B.; Ouarti, N.; Silva, P. L.; Blagoeva, I. B.; El Seoud, O. A.; Ruasse, M.-F. *Langmuir* **2003**, *19*, 10666−10672).
(29) Fernandez, M. S.; Fromherz, P. *J. Phys. Chem.* **1977**, *81*, 1755−1761.
(30) Exner, O. In *Correlation Analysis in Chemistry*; Chapman, N. B., Shorter, J., Eds.; Plenum: London, 1978; pp 439−540.

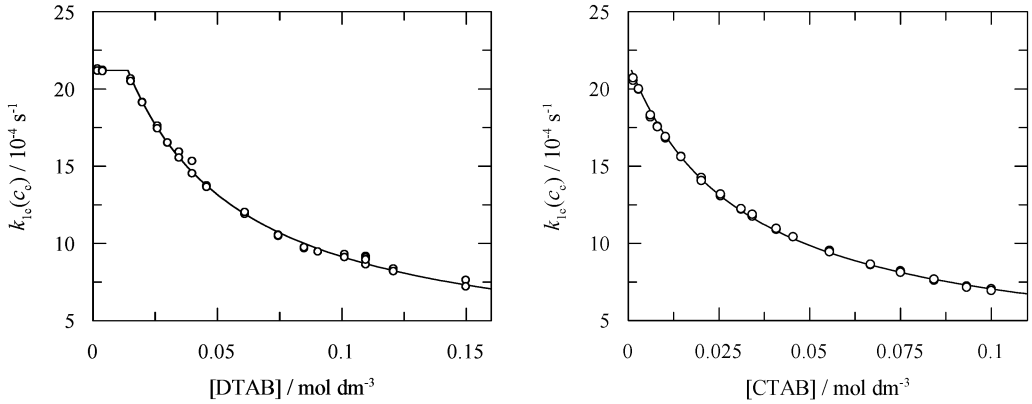


FIGURE 1. Rate constants of hydrolysis of **1c** at 298.15 K in solutions containing micelles of DTAB (left) and CTAB (right).

TABLE 2. Overview of Micellar Rate Constants of Hydrolysis and Micellar Binding Constants[a] of Para-Substituted 1-Benzoyl-1,2,4-triazoles 1a−f at 298.15 K

	$k_{x,CTAB}/10^{-4}$ s^{-1}	$k_{x,DTAB}/10^{-4}$ s^{-1}	$K_{x,CTAB}$[b]$/10^3$ dm^3 mol^{-1}	$K_{x,DTAB}$[c]$/10^3$ dm^3 mol^{-1}
1a	0.34 ± 0.03	0.25 ± 0.04	9.3 ± 0.3	3.1 ± 0.2
1b	0.78 ± 0.08	0.70 ± 0.06	10.3 ± 0.4	3.4 ± 0.1
1c	2.5 ± 0.2	2.4 ± 0.3	3.44 ± 0.07	1.5 ± 0.1
1d	5.4 ± 0.2	6.67 ± 0.10	13.9 ± 0.4	4.2 ± 0.1
1e	7.0 ± 0.1	8.4 ± 0.2	21.0 ± 0.3	6.0 ± 0.1
1f	67 ± 3	74 ± 12	6.4 ± 0.3	1.4 ± 0.2

[a] Cmcs set to 0.9 and 14.0 mM for CTAB and DTAB, respectively. These are the average values of the cmcs determined from initial curve-fitting with unrestricted cmcs. [b] Based on an aggregation number of 110.[31] [c] Based on an aggregation number of 70.[31]

TABLE 3. Relative Rate Constants of Hydrolysis of 1a−f Taking Place in Micelles of DTAB and CTAB at 298.15 K

	CTAB		DTAB	
	$k_{x,mic}/k_x(m_c = 0)$	$\ln[k_{x,mic}/k_x(m_c = 0)]$	$k_{x,mic}/k_x(m_c = 0)$	$\ln[k_{x,mic}/k_x(m_c = 0)]$
1a	0.08	−2.5 ± 0.1	0.06	−2.8 ± 0.2
1b	0.08	−2.5 ± 0.1	0.07	−2.6 ± 0.1
1c	0.12	−2.14 ± 0.06	0.12	−2.1 ± 0.3
1d	0.15	−1.90 ± 0.04	0.19	−1.68 ± 0.02
1e	0.16	−1.82 ± 0.02	0.20	−1.63 ± 0.02
1f	0.24	−1.42 ± 0.03	0.27	−1.3 ± 0.2

completely miscible with water at 298.15 K. In addition, widely accepted micelle models suggest that on average about 2−3 methylene units are in contact with water.[2] The effects of ionic headgroups and alkyl tails as mimicked by TMAB and 1-propanol, respectively, have to be distinguished. Ideally, trends in sensitivity toward the presence of these two compounds should be different within the series of hydrolytic probes. By analogy with 1:1 interactions in (aqueous) solutions (see ref 33 for short reviews), we quantify rate-retarding effects exerted by the two mimicking compounds using the slopes of plots of the logarithm of the relative rate constant of hydrolysis as a function of molality of cosolute m_c, eq 3.[34,35]

$$\ln[k(m_c)/k(m_c = 0)] = \frac{2}{RTm_o^2}G(c)m_c - NM_l\phi m_c \quad (3)$$

Here $k(m_c)$ is the (pseudo-)first-order rate constant for hydrolysis in an m_c molal aqueous solution of cosolute c; $k(m_c = 0)$ is the rate constant in the absence of added cosolute, R is the gas constant, and T is the absolute temperature. G(c) is the difference $[g_{cx} - g_{c‡}]$ in interaction Gibbs energies between the cosolute c and the reactants x on one hand and the cosolute c and the activated complex ‡ on the other hand. M_l is the molar mass of water, N is the number of water molecules involved in the rate-determining step, and ϕ is the practical osmotic coefficient for the aqueous solution where the molality of added solute is m_c. In this study, N equals 2 (vide supra). Since the solutions are very dilute, ϕ can be taken as unity; m_o, 1 mol kg^{-1}, is the molality of the solute reference state. In short, $NM_l\phi m_c$ gives the change in water activity upon addition of m_c

(31) van Os, N. M.; Haak, J. R.; Rupert, L. A. M. *Physico-Chemical Properties of Selected Anionic, Cationic and Nonionic Surfactants*; Elsevier: Amsterdam, 1993.

(32) Hydrophobic interactions are rather dependent on size and shape of the hydrophobic (parts of) molecules involved; see e.g.: Southall, N. T.; Dill, K. A. *J. Phys. Chem. B* **2000**, *104*, 1326−1331. We therefore restricted our choice of alcohols for our mimicking solution to linear alcohols. The actual choice of linear alcohol is expected to be unimportant as all short-chain linear alcohols retard the hydrolysis reactions of activated amides in similar ways following an additivity scheme (see ref 35 and the following: Buurma, N. J.; Pastorello, L.; Blandamer, M. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **2001**, *123*, 11848−11853).

(33) (a) Engberts, J. B. F. N.; Blandamer, M. J. *J. Phys. Org. Chem.* **1998**, *11*, 841−846. (b) Otto, S.; Engberts, J. B. F. N. *Org. Biomol. Chem.* **2003**, *1*, 2809−2820.

(34) Blokzijl, W.; Engberts, J. B. F. N.; Blandamer, M. J. *J. Phys. Chem.* **1987**, *91*, 6022−6027.

(35) Blokzijl, W.; Engberts, J. B. F. N.; Blandamer, M. J. *J. Am. Chem. Soc.* **1990**, *112*, 1197−1201.

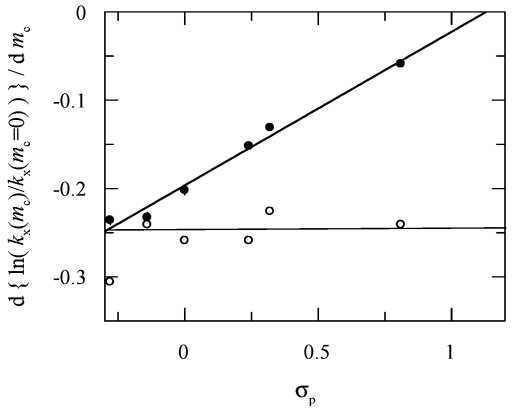


FIGURE 2. Rate-retarding effects of 1-propanol (●) and TMAB (○) on the hydrolysis of probes **1a**−**f** at 298.15 K as a function of Hammett substituent constants.

TABLE 4. Concentration Dependence (kg mol^{-1}) of Rate-Retarding Effects of 1-Propanol and TMAB on the Hydrolysis of Substituted 1-Benzoyl-1,2,4-triazoles 1a−f at 298.15 K

	$\partial\ln\{k_x(m_{1-\text{propanol}})/k_x(m_c=0)\}/\partial m_{1-\text{propanol}}$	$\partial\ln\{k_x(m_{\text{TMAB}})/k_x(m_c=0)\}/\partial m_{\text{TMAB}}$
1a	−0.236 ± 0.005	−0.306 ± 0.015
1b	−0.232 ± 0.006	−0.240 ± 0.007
1c	−0.201 ± 0.005	−0.258 ± 0.006
1d	−0.151 ± 0.003	−0.259 ± 0.007
1e	−0.131 ± 0.003	−0.226 ± 0.002
1f	−0.058 ± 0.002	−0.240 ± 0.007

molal of a cosolute and $2/RTm_o^2G(c)m_c$ gives the intersolute interactions upon addition of m_c molal of a cosolute. Equation 3 is used to obtain $G(c)$ values which may be subsequently analyzed using a group-additivity approach. For the present case, it should be noted that $G(c)$ often follows a group-additivity pattern and that interactions with different cosolutes are expected to be additive.[33] For dilute solutions for which eq 3 is valid, $\ln[k(m_c)/k(m_c=0)]$ varies linearly with molality m_c.

In the present case, the rate-retarding effects of TMAB and 1-propanol were determined in the ranges from 0 up to (at most) 5 mol kg^{-1} and from 0 up to 3.6 mol kg^{-1}, respectively (Table 4).

The necessary difference in sensitivity trends exists. Whereas the variation in the effect of TMAB on the hydrolysis of **1a**−**f** is relatively modest, the rate-retarding effect of 1-propanol varies substantially with the Hammett substituent constant (Figure 2).

This difference allows the calculation of individual molalities of the headgroup mimic and the tail mimic as required for a solution mimicking the micellar Stern region. These calculated molalities are assumed to reflect the relative importance of ionic interactions and hydrophobic interactions in the Stern region. For a graphical solution, the rate-retarding effect of 1-propanol on the hydrolysis reactions decreases roughly linearly with substituent parameter σ_p. Hence, there is a hypothetical hydrolytic probe with a (hypothetical) substituent for which hydrolysis is not retarded by 1-propanol. This hypothetical substituent has a σ_p of about 1.13. A plot of $\ln(k_{x,mic}/k_x(m_c=0))$ as a function of σ_p can now be divided into two parts, viz. a part where rate retardation is caused by hydrophobic interactions and a part where rate

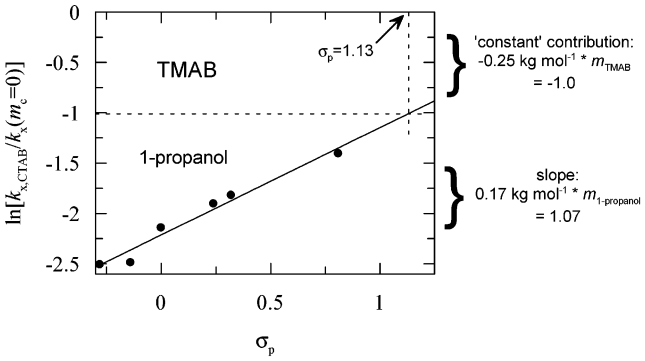


FIGURE 3. Relative rate-retarding effects of CTAB micelles on the hydrolysis of **1a**−**f** at 298.15 K as a function of Hammett substituent constant. Dotted line indicates the division between rate-retarding effects attributed to interactions with ionic surfactant headgroups as modeled by TMAB (upper section) and rate-retarding effects attributed to interactions with surfactant alkyl tails as modeled by 1-propanol (lower section). The dotted and the solid lines cross at $\sigma_p = 1.13$ (see text for details).

retardation is caused by interactions with ionic headgroups (Figure 3).

Hydrolysis of a probe with a substituent with $\sigma_p = 1.13$ is expected to be solely retarded by ionic interactions. Because rate retardation by ionic interactions as modeled by TMAB is approximately constant for all hydrolytic probes, the horizontal dotted line at $\ln[k_{x,CTAB}/k_x(m_c=0)] = -1.0$ indicates the constant "ionic contribution" to the rate-retarding effect for all hydrolytic probes. As the rate retardation (expressed in terms of logarithm of the relative rate retardation; vide supra) by ionic interactions is approximately −0.25 kg mol^{-1} for TMAB, the micellar rate-retarding effect attributed to ionic interactions of −1.0 corresponds to a model solution of −1.0/−0.25 mol kg^{-1} = 4 mol kg^{-1} in TMAB. The slope of the remainder of the rate-retarding effect, attributed to hydrophobic interactions, as a function of substituent parameter equals 1.07. As a slope of 0.17 is expected for a 1 mol kg^{-1} solution, we estimate a model solution for the micellar Stern region to be approximately 1.07/0.17 = 6 mol kg^{-1} in 1-propanol.

An alternative approach uses equations used in the study of 1:1 interactions in aqueous solutions.[34] The rate-retarding effect in an aqueous solution containing 1-propanol and TMAB can be described as the sum of effects caused by added TMAB and 1-propanol:

$$\frac{\partial\ln\left[\dfrac{k_x(m_{1-\text{propanol}})}{k_x(m_c=0)}\right]}{\partial m_{1-\text{propanol}}} m_{1-\text{propanol}} + \frac{\partial\ln\left[\dfrac{k_x(m_{\text{TMAB}})}{k_x(m_c=0)}\right]}{\partial m_{\text{TMAB}}} m_{\text{TMAB}} = \ln\left[\frac{k_{x,\text{mic}}}{k_x(m_c=0)}\right] \quad (4)$$

Equation 4 is more conveniently written in the form of eq 5:

$$a_{x,1-\text{propanol}} m_{1-\text{propanol}} + a_{x,\text{TMAB}} m_{\text{TMAB}} = c_x \quad (5)$$

Here, $a_{x,1-\text{propanol}}$ is the derivative of the logarithm of the

TABLE 5. Molalities and Concentrations[a] of 1-Propanol and TMAB in Soln.1 for Binding Sites of 1a−f in Micelles of DTAB and CTAB

	DTAB		CTAB	
	m_c/mol kg^{-1}	c_c/mol dm^{-3}	m_c/mol kg^{-1}	c_c/mol dm^{-3}
1-propanol	9.3 ± 0.9	5.1	5.0 ± 0.5	2.6
TMAB	1.5 ± 0.6	0.8	4.9 ± 0.3	2.6
water		30		29

[a] Concentrations were calculated using the (experimentally determined) densities of the "first-order solutions" Soln.1 at 298.15 K (densities of the first-order solutions for CTAB and DTAB are 1.079 and 0.975 g cm^{-3}, respectively).

relative rate constant with respect to molality of 1-propanol, $a_{x,TMAB}$ is the same derivative with respect to the molality of TMAB, and c_x is the logarithm of the relative micellar rate constant. For a model solution consistently describing the micellar Stern region of the micelles formed by a certain surfactant, this equation should hold for all the hydrolytic probes in combination with this surfactant. Hence, for a given surfactant, there is a model solution of $m_{1-propanol}$ mol kg^{-1} in 1-propanol and m_{TMAB} mol kg^{-1} in TMAB in which the hydrolysis reactions of *all* hydrolytic probes **1a**−**f** are retarded to the same extent as in the micellar Stern region. Hence, for every surfactant a set of linear equations is given by eq 5. In its extended form, these equations form the matrix given in eq 6:

$$\begin{bmatrix} a_{MeO,1-propanol} & a_{MeO,TMAB} \\ a_{Me,1-propanol} & a_{Me,TMAB} \\ a_{H,1-propanol} & a_{H,TMAB} \\ a_{Cl,1-propanol} & a_{Cl,TMAB} \\ a_{F_3CO,1-propanol} & a_{F_3CO,TMAB} \\ a_{NO_2,1-propanol} & a_{NO_2,TMAB} \end{bmatrix} \begin{bmatrix} m_{1-propanol} \\ m_{TMAB} \end{bmatrix} = \begin{bmatrix} c_{MeO} \\ c_{Me} \\ c_H \\ c_{Cl} \\ c_{F_3CO} \\ c_{NO_2} \end{bmatrix} \quad (6)$$

Overdetermined (not exact) matrix systems of the form in eq 6 can be solved using singular value decomposition.[36] The entries in vector c_x and matrix $a_{x,c}$ are given in Tables 3 and 4, respectively. With application of the singular value decomposition method, a calculated model solution mimicking the micellar Stern region of a CTAB micelle is described in Table 5. The solution describes a "first-order solution" of eq 6, based entirely on extrapolated 1:1 interactions. This solution will be referred to as Soln.1.

The salt concentrations in Table 5 are lower than those in the concentrated salt solutions described in our previous paper[1] where the salt was taken as the sole origin of rate retardation. Nevertheless, the salt concentrations match the calculated concentration ranges given in our previous report but now at the lower end of the calculated range. In fact, the value of 2.6 mol dm^{-3} is in reasonable agreement with the concentrations of bromide anions (1.6 mol dm^{-3}) and ionic headgroups (2.0 mol dm^{-3} assuming a counterion binding of 0.8) as determined by the Romsted group using their arenediazonium probe.[15] Rate constants for hydrolysis of **1a**−**f**[37] and $E_T(30)$ value were

SCHEME 2

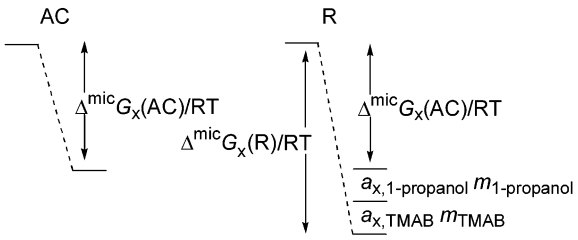


TABLE 6. Comparison of Soln.1 and the Micellar System for CTAB at 298.15 K

	$k_{x,mic}$ / 10^{-4} s^{-1}	$k_{x,Soln.1}$ / 10^{-4} s^{-1}	$k_{x,Soln.1}^{calc}$/ 10^{-4} s^{-1} [a]	$\ln(k_{x,mic}/k_{x,Soln.1})$
1a	0.34 ± 0.03	0.54 ± 0.04	0.28	−0.463
1b	0.78 ± 0.08	1.45 ± 0.03	0.92	−0.620
1c	2.5 ± 0.2	3.71 ± 0.24	2.21	−0.399
1d	5.4 ± 0.2	8.0 ± 0.1	4.76	−0.402
1e	7.0 ± 0.1	10.28 ± 0.07	7.41	−0.386
1f	67 ± 3	77.7 ± 5.6	64.6	−0.132

[a] Calculated using eq 6.

determined for the solution mimicking CTAB made according to Table 5, i.e. in Soln.1(CTAB) (Table 6).

According to Table 6, rate constants for hydrolysis of individual probes in the model solution are only slightly higher than those in the CTAB Stern region. This discrepancy is attributed to the fact that hydrolysis data for **1a**−**f** in binary aqueous solutions of TMAB or 1-propanol as determined at intermediate molalities have been extrapolated to higher molalities. In addition, the final solution is a ternary solution, introducing further deviations from the extrapolations for binary solutions. An encouraging observation is that the $E_T(30)$ value for the mimicking solution (55.8 kcal mol^{-1}) is in far better agreement with the value for CTAB micelles (53.5 kcal mol^{-1}) than the $E_T(30)$ values of the model solutions containing only TMAB.[1] Further, we calculated the expected micellar (CTAB and DTAB) rate constant of hydrolysis for **2**. Using the molalities (and concentrations) determined here, together with the G(c) value of 1-propanol for hydrolysis of **2** determined previously[35] and the dependence of the hydrolysis of **2** in aqueous solutions containing TMAB on molarity (Figure 2 in ref 1), the rate constant of the hydrolysis of **2** in the Stern region of CTAB micelles is expected to be (1.4 ± 0.4) × 10^{-4} s^{-1}. Experimentally, a micellar rate constant of (0.67 ± 0.08) × 10^{-4} s^{-1} is observed.[1] Similarly, the rate constant for the hydrolysis of **2** in DTAB micelles is expected to be (1.1 ± 0.3) × 10^{-4} s^{-1}, in good agreement with the experimental micellar rate constant[1] of (1.26 ± 0.05) × 10^{-4} s^{-1}. In other words, the model predicts reasonably well reaction rates for reactions that were not used in the development of the model.

Using the results of the analysis, we describe the micellar binding and micellar inhibition in a single scheme (Scheme 2, different contributions not drawn to scale).

Both reactant (R) and activated complex (AC) bind to the micelle in the Stern region (Table 2). However, R binds much more strongly than AC, causing the rate retardation. We divide the Gibbs energy of binding of R to the micelle into a "dynamic" part, causing rate effects,

(36) Atkinson, K. E. *An Introduction to Numerical Analysis*; 2nd ed.; Wiley: New York, 1988.

(37) The 1-propanolysis of **1a**−**f** is expected to make a negligible contribution to the observed rate constants (see ref 35).

and a "passive" part, not causing rate effects (cf. a related division into passive and dynamic interactions in ref 38, for the present case the passive interactions correspond to K^{AC}). Using eq 6, the dynamic part has been divided into rate-retarding effects caused by interactions with ionic groups (as quantified by $a_{x,TMAB}m_{TMAB}$) and effects caused by interactions with hydrophobic groups (as quantified by $a_{x,1-propanol}m_{1-propanol}$). For probes for which the dynamic part of the Gibbs energy of binding to the micelle is the same (i.e. probes with the same kinetic sensitivity toward hydrophobic and ionic interactions but for which the passive part is different), a linear relation between pK_m and pK^{AC} with a slope of 1 is expected. Indeed, such a linear relation is found for probes of which only the hydrophobicity is increased by elongating an alkyl chain remote from the reaction center.[39] Similarly, the reason for the absence of a correlation between rate-retarding effects, micellar binding constants, and hydrophobicity of the surfactants constituting the micelle as found in this study stems from different and uncorrelated passive and dynamic contributions to the Gibbs energy of binding to the micelles.

The present analysis, separating the contributions of hydrophobic and ionic interactions, uses the differences in rate-retarding effects caused by hydrophobic interactions and ionic interactions. However, additional effects causing differences in rate-retarding effects have not been included in the present model. Three of these effects are readily identified, and their source, effect, and importance can be estimated.

First, different hydrolytic probes could bind in different zones of the micelle (or their distribution over different zones of the micelle could change[1]) and therefore experience different interactions. However, the kinetic probes used in this study are structurally similar and are all expected to reside in the micellar Stern region.[11] Hence, any difference in rate effect caused by a difference in binding locations is expected to be of minimal importance.

Second, the electrostatic nonneutrality of the micellar Stern region can (de)stabilize charges developing in the activated complex. In the present case, the partial negative charge on the AC will be stabilized by the effectively cationic Stern region. This effect will be modified by other factors (de)stabilizing the partial negative charge, e.g. (de)stabilization by substituent effects. Hence, different probes can be differently stabilized by the cationic nature of the micellar Stern region.

Third, the local pH in the Stern region may be different from the bulk pH. The local pH on the micellar surface can be calculated from the bulk pH and the micellar surface charge using the Poisson−Boltzmann equation.[29] For a bulk pH of 4.0, the pH in the micellar Stern region of CTAB is calculated to be approximately 6.5. Experiments using **1e** indicate that hydroxide-ion catalyzed hydrolysis contributes less than 5% to the rate constant of hydrolysis of **1e** in the "second-order solution" (vide infra) at pH 6.5. This suggests that, for the system studied here, hydroxide-ion catalyzed hydrolysis as a result of the different pH is not an important factor.

Notwithstanding the fact that conclusions about the micellar binding sites can be drawn from the first-order solution, it would be useful to have a real solution accurately reproducing rate constants in the micellar Stern region. In the study of bimolecular reactions occurring in the Stern region, it is often especially difficult to determine independently binding constants for both reactants and the micellar rate constant.[40−42] We therefore extended the model for CTAB to prepare a solution that includes the nonlinear rate-retarding effects at high molalities of TMAB and 1-propanol (vide supra). We determined these rate-retarding effects at high molality in much the same way as was used at low molality. Instead of using rate constants in water without added cosolute as reference points, rate constants in Soln.1, $k_x(m_{TMAB} = 4.85, m_{1-propanol} = 5.00)$, denoted as k_x(Soln.1), were taken as reference points. Rate constants for hydrolysis of the hydrolytic probes in the presence of high molalities of TMAB and 1-propanol, $k_x(m_{TMAB}, m_{1-propanol})$, were determined in solutions where TMAB and 1-propanol molalities were around 4.85 and 5.00 mol kg^{-1}, respectively, i.e. around the molalities in Soln.1.

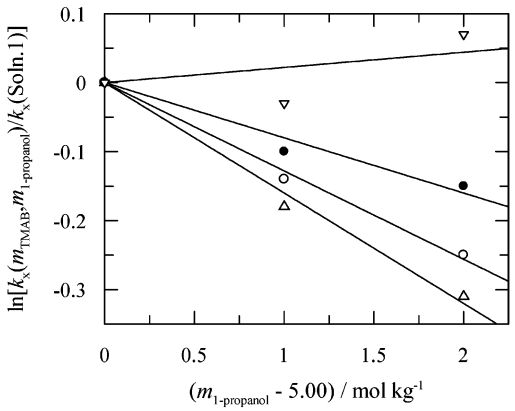


FIGURE 4. Representative examples of the rate-retarding effect of (additional) added 1-propanol on the hydrolysis of **1a** (○), **1b** (△), **1d** (●), and **1f** (▽) at 298.15 K at a constant TMAB molality m_{TMAB} of 4.85 mol kg^{-1}, using Soln.1 as reference.

Plots of $\ln[k_x(m_{TMAB}, m_{1-propanol})/k_x(\text{Soln.1})]$ as a function of 1-propanol molality around the 1-propanol molality of Soln.1 and at a constant m_{TMAB} of 4.85 mol kg^{-1} are not linear (Figure 4).

Nevertheless, a linear fit, forced through the reference point provided by Soln.1, was used to obtain $\delta\ln[k_x(4.85, m_{1-propanol})/k_x(\text{Soln.1})]/\delta m_{1-propanol}$ (denoted $a_{x,1-propanol}^{Soln.1}$). For the dependence on m_{TMAB}, only one additional data point (for every probe) was determined as an indication of $\delta\ln[k_x(m_{TMAB}, 5.00)/k_x(\text{Soln.1})]/\delta m_{TMAB}$ (denoted $a_{x,TMAB}^{Soln.1}$). The calculated slopes are given in Table 7.

An improved estimate of the molalities for a model solution accurately reproducing micellar rate constants can be determined starting from the first-order solution. Equation 6 with $c_x = \ln(k_{x,mic}/k_x(\text{Soln.1}))$ (the residual of the first-order model solution) and with $a_{x,1-propanol}$ and $a_{x,TMAB}$ set to $a_{x,1-propanol}^{Soln.1}$ and $a_{x,TMAB}^{Soln.1}$ (Table 7),

(38) Kirby, A. J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 707−724.
(39) Tee, O. S.; Yazbeck, O. J. *Can. J. Chem* **2000**, *78*, 1100−1108.
(40) Rispens, T.; Engberts, J. B. F. N. *J. Org. Chem.* **2002**, *67*, 7369−7377.
(41) Rispens, T.; Engberts, J. B. F. N. *J. Org. Chem.* **2003**, *68*, 8520−8528.
(42) It is expected that the micellar rate constants as reported in refs 40 and 41 will be reasonably well reproduced by the model solutions reported here. This is expected because water concentrations are less than 30 M in all the presented model solutions.

TABLE 7. Rate-Retarding Effects of 1-Propanol and TMAB on the Hydrolysis of Substituted 1-Benzoyl-1,2,4-triazoles 1a−f at 298.15 K for Molalities around Soln.1

	$a_{x,1-propanol}^{Soln.1}$/ kg mol^{-1}	$a_{x,TMAB}^{Soln.1}$/ kg mol^{-1}
1a	−0.128 ± 0.005	−0.13[a]
1b	−0.160 ± 0.008	−0.19
1c	−0.160 ± 0.008	−0.19
1d	−0.080 ± 0.008	−0.18
1e	−0.078 ± 0.005	−0.22
1f	+0.022 ± 0.019	−0.19

[a] Error has been set to 0.01 kg mol^{-1} for all entries in this column.

respectively, yields a correction term for the "first-order solution" equal to +2.7 ± 0.9 mol kg^{-1} for 1-propanol and +0.8 ± 0.4 mol kg^{-1} for TMAB. Therefore the "second-order solution" (Soln.2) should contain 7.7 ± 0.9 mol kg^{-1} 1-propanol and 5.7 ± 0.4 mol kg^{-1} TMAB. We tested this second-order solution. The rate constant for hydrolysis of **1e**, which is most sensitive to ionic interactions, equals 7.6 × 10^{-4} s^{-1}, in good agreement with the micellar rate constant of (7.0 ± 0.1) × 10^{-4} s^{-1}. The $E_T(30)$ value, which is most sensitive to hydrophobic interactions, equals 54.4 ± 0.2 kcal mol^{-1}, in reasonable agreement with the micellar value[1] of 53.5 kcal mol^{-1} (90% of the decrease in excitation energy accounted for).[43] In addition, the rate constant for hydrolysis of **2** in Soln.2 is (9.5 ± 0.5) × 10^{-5} s^{-1}, in reasonable agreement with the micellar rate constant of (6.7 ± 0.8) × 10^{-5} s^{-1} (88% of the increase in Gibbs energy of activation accounted for). Therefore, reasonable estimates of micellar rate constants and even micropolarity, as determined using the $E_T(30)$ probe, can be obtained using the present model solution for CTAB. Furthermore, the results obtained for **2** and the $E_T(30)$ probe (both were not used in the optimization of our model) suggest that this can also be done for reactions and properties that were not included in the construction of the model. Hence, the present model is the first to be able to reproduce a diverse range of medium-controlled properties of the micellar Stern region and it indicates that other effects that were not included in the analysis (vide supra) play only a minor role.

The present model is not limited to alkyltrimethylammonium bromide surfactants. Comparable model solutions can also be determined for other surfactants, both micelle- and vesicle-forming, provided the salt mimicking the micellar headgroups is appropriate. Availability of solutions mimicking the micellar Stern region is especially helpful for determining factors underlying either micellar catalysis or inhibition of bimolecular (or higher molecularity) reactions. Despite the emphasis on reaction kinetics in this study, virtually any property of the micellar Stern region can be used in similar analyses.

(43) The relatively high sensitivity of the $E_T(30)$ probe toward hydrophobic interactions provides a possibility for a quick test of the nature of the micellar Stern region. The $E_T(30)$ probe can be used mainly for the interactions with the alkyl tails whereas **1e** is mainly suitable for the interactions with the ionic headgroups. This results in a 2 × 2 matrix with one row strongly dependent on TMAB molality and one row mainly dependent on 1-propanol molality, yielding a reasonable first indication of the Stern region as a reaction medium.

Conclusions

The failure of concentrated salt solutions to reproduce polarity-related properties of the micellar Stern region[1] indicated the necessity of expanding our previous model mimicking the Stern region in such a way that rate-retarding hydrophobic interactions are correctly taken into account. For DTAB and CTAB, this has been accomplished by modeling the micellar Stern region using an aqueous solution containing both 1-propanol, mimicking hydrophobic surfactant tails, and TMAB, mimicking ionic surfactant headgroups. The molalities of TMAB and 1-propanol in these solutions can be determined graphically and mathematically, using singular value decomposition. We distinguish two "types" of model solutions, viz. first-order and second-order solutions. First-order solutions are determined from the rate-retarding effects of 1-propanol and TMAB at intermediate molalities and indicate the relative importance of ionic and hydrophobic groups in the micellar Stern region. Second-order solutions can be derived from first-order solutions and take into account the nonlinear rate retardations at high molalities of cosolutes. Second-order solutions can be used to obtain estimates of micellar rate constants for reactions of which the micellar rate constants cannot be determined directly. The present approach can be used for both micellar and vesicular systems and probably has an even wider applicability.

Experimental Section

Substituted 1-benzoyl-1,2,4-triazoles (**1a**−**f**) and 1-benzoyl-3-phenyl-1,2,4-triazole (**2**) were synthesized according to literature procedures.[44] The $E_T(30)$ probe was kindly provided by Prof. Dr. Chr. Reichardt. Micellar solutions were 1 × 10^{-4} mol dm^{-3} in HCl, and model compound solutions were acidified to pH 4 to achieve conditions for pH-independent hydrolysis. All solutions were made in water that was distilled twice in an all-quartz apparatus. Surfactants and salts were dried before use. If solutions were made volumetrically, the mass of all components of the solutions was determined to know both solute and solvent concentration. If model solutions were made by weight, the density was determined. Reactions were followed at 260, 262, 252, 262, 253, and 262 nm for **1a**−**f**, respectively, and at 273 nm for **2**, at 298.15 ± 0.2 K for at least 6 half-lives. Good to excellent pseudo-first-order kinetics were obtained, the error in the rate constants being 2% or less for the micellar solutions and the dilute solutions but up to 10% for the concentrated solutions.

The probes were injected as 6 μL of a stock solution of **1a**−**f** or 2−5 μL of a stock solution of **2** in cyanomethane into a 1 cm quartz cuvette of ca. 2.5 mL yielding a total probe concentration during the reaction of ca. 10^{-5} mol dm^{-3}. These concentrations were chosen to have absorbance changes not larger than 0.6.

The measurements involving the $E_T(30)$ probe were performed at pH 11. The $E_T(30)$ probe was injected as <6 μL of a stock solution of the solvatochromic probe in EtOH.

The singular value decomposition method was used as implemented in Mathcad 2001 Professional by Mathsoft Inc.

Acknowledgment. Marie Jetta den Otter is gratefully acknowledged for her contribution to this work.

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(44) (a) Staab, H. A.; Lüking, M.; Dürr, F. H. *Chem. Ber.* **1962**, *95*, 1275−1283. (b) Karzijn, W. *The water- and hydroxide-ion catalyzed hydrolysis of 1-acyl-1,2,4-triazoles*. Ph.D. Thesis, University of Groningen, 1979. (c) Mooij, H. J.; Engberts, J. B. F. N.; Charton, M. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 185−189.